

Advanced primary carcinoma of the Bartholin gland: Report of 18 patients

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Summary

Conservative surgery plus radiotherapy for vulvar cancer has been established as a therapeutic alternative to extensive radical surgery and produces a similar cumulative 5-year survival. We retrospectively analyzed the cases of 18 patients with advanced primary carcinoma of the Bartholin gland treated with wide local excision (WLE) or radical vulvectomy and lymphadenectomy followed by radiotherapy (RT) at the University of Texas M. D. Anderson Cancer Center from January 1978 through December 1990.

All patients have been observed for a minimum of 7 months (maximum follow-up, 15 years; median follow-up, 9 years). Of the 18 patients, 7 were treated with wide local excision (WLE) followed by radiation therapy (RT) (Group I), 9 had radical vulvectomy (RV) followed by RT to the vulvar and inguinal-femoral and pelvic node areas (Group II), and 2 were treated with RT alone after biopsy of the tumor (Group III).

The 5-year disease-free survival rates were 86%, 78%, and 50% for groups I, II, and III, respectively, and 83% for the whole group. Of 2 patients treated with RT alone, one lived for 6 years with no evidence of disease, and the other lived for 20 months. The rate of local tumor control was 100% for all three treatment groups. There were no significant differences among the treatment groups in rate of primary tumor control or 5-year disease-free survival rate ($p=0.1300$).

The present study demonstrated WLE followed by RT is the best treatment for advanced primary carcinoma of the Bartholin gland. Less radical surgery plus RT produces good long-term survival and has fewer complications.

Key Words: Bartholin gland carcinoma; Radical vulvectomy; Radiotherapy; Wide local excision.

Introduction

Primary carcinoma of the Bartholin gland is an uncommon lesion that accounts for 2% to 7% of vulvar neoplasms and for less than 1% of all female genital tract malignancies [1]. Various therapeutic modalities have been suggested, such as pelvic exenteration, radical vulvectomy and bilateral lymphadenectomy, radical hemivulvectomy, wide excision, and radiotherapy with or without surgery [2-5]. Conservative surgery plus radiotherapy for vulvar cancer has been established as a therapeutic alternative to extensive radical surgery and produces a similar cumulative 5-year survival [3-8]. This is a retrospective analysis of 18 patients with advanced primary carcinoma of the Bartholin gland treated with wide local excision or radical vulvectomy and lymphadenectomy followed by radiotherapy. Our aim is to reemphasize that for these patients, less radical surgery followed by radiotherapy retains the long-term survival of more radical surgery and has less morbidity.

Materials and Methods

From January 1978 through December 1990, 18 patients ranging in age from 42 to 93 years (median, 66) who had advanced Bartholin gland carcinoma were treated with different modalities at the University of Texas M. D. Anderson Cancer

Center. Patients were staged according to guidelines of the International Federation of Gynecology and Obstetrics (FIGO). Sixteen patients had stage III disease and two had stage IV disease.

For the current study, all radiation oncology and hospital records were retrospectively reviewed. All the information was coded on computer-compatible forms and analyzed by a computer program with multiple cross-reference checks to ensure reliability of the data.

A biomedical statistical program was used for data analysis [9]. All patients have been observed for a minimum of seven

Table 1. — Characteristics of study patients

Characteristics	Group I WLE + Postop RT (n:7)	Group II RV + Postop RT (n:9)	Group III RT alone (n:2)	Total Group (n:18)
Age at diagnosis	68	67	78	69
Tumor type				
SCC	3	7	2	12(67)
AC	4	2	—	6 (33)
Tumor stage				
III	5	8	1	16 (89)
IV	1	—	1	2 (11)
Tumor grade				
I	1	1	—	2 (11)
II	2	3	—	5 (28)
III	4	5	2	49 (61)

WLE: Wide local excision; **RV:** Radical vulvectomy; **RT:** Radiotherapy; **SCC:** Squamous cell carcinoma; **AC:** Adenocarcinoma; **Parentheses = %**

Revised manuscript accepted for publication September 12, 2000

Table 2. — Analysis of patients who underwent lymphadenectomy

Patient	Surgery and Disease	Inguinal Lymph Node Dissection	Pathology	Survival Duration (months)
JM	RV-Stage III	Right superficial and deep LND	Negative node	168-alive
LC	RV-Stage III	Left superficial LND	Positive node	24-died of DM
SM	RV-Stage III	Left superficial and deep LND	Positive node	108-alive
DW	RV-Stage III	Left superficial and deep LND	Positive node	168-alive
RH	RV-Stage III	Left superficial and deep LND	Negative node	150-alive
ES	RV-Stage III	Left superficial and deep LND	Positive node	168-alive
AJC	RV-Stage III	Bilateral superficial and deep LND	Negative node	20-died of DM
AJL	RV-Stage III	Right superficial and deep LND	Negative node	72-died NED
EP	WLE-Stage III	Bilateral superficial and deep LND	Negative node	180-alive
JC	WLE-Stage III	Bilateral superficial and deep LND	Positive node	154-alive
VMC	WLE-Stage-IVA	Left superficial LND	Positive node	7-died of DM

RV: Radical vulvectomy; WLE: Wide local excision; LND: Lymph node dissection; DM: Distant metastasis

months (maximum follow-up, 15 years; median follow-up, 9 years). Of the 18 patients, seven were treated with wide local excision (WLE) followed by radiation therapy (RT) (Group I), nine had radical vulvectomy (RV) followed by RT to the vulvar and inguinal-femoral and pelvic node areas (Group II), and two were treated with RT alone after biopsy of the tumor (Group III) (Table 1).

Lymphadenectomy (8 unilateral and 3 bilateral) was performed on 11 patients; the depth of the lymph node dissection was superficial in two patients and both superficial and deep in nine (Table 2). The patients were treated in the supine position. Megavoltage irradiation (6 and 18 MV photons) was used, either with equal or unequal loading. An additional dose was delivered to the primary tumor site with an external beam or with interstitial implants. Doses ranged from 40 to 70 Gy depending on the volume of tumor to be treated; daily fractions ranged from 1.6 to 2.0 Gy five days per week. All data for overall and disease-free survival and local control were determined using the Berkson and Gage lifetable method [10]; P values were computed by the Lee and Desu method [11].

Results

Patient characteristics: Of the 18 patients, 12 (67%) had squamous cell carcinoma, and six (33%) had adenocarcinoma. Table 1 presents the patient characteristics, including age at diagnosis and tumor type, stage, and grade by treatment group. Table 2 shows an analysis of patients who underwent lymphadenectomy. Eleven of 18 patients underwent lymphadenectomy, and six had nodal metastases.

Recurrence analysis: Table 3 presents the anatomic sites of recurrence for the various treatment groups. Disease recurrences were classified as local (affecting the vulva itself), regional (affecting the inguinal-femoral nodes), or distant. Intrapelvic nodes are considered "distant" rather than regional. There were no local recurrences in any treatment group. Three of 18 patients had distant metastases.

Survival Results: Table 4 presents the post-therapy survival duration for the 18 patients. Of two patients treated with RT alone, one lived for six years with no evidence of disease, and the other lived for 20 months. The 5-year disease-free survival was 86%, 78% and 50% for groups I, II, III, respectively, and 83% for the whole group (Table 5).

Table 3. — Bartholin gland carcinoma (MDACC 1978-1990): Disease recurrence and survival by treatment group

	Group I WLE + RT (n:7)	Group II RV + RT (n:9)	Group III RT alone (n:2)	Total Group (n:18)
Disease status				
NED	7	7	1	15 (83)
LR	—	—	—	—
DM	1	1	1	3 (17)
LR+DM	—	—	—	—
Survival Status				
Alive	7	6	—	13 (72)
Deceased	1	2	2	5 (28)

MDACC: M. D. Anderson Cancer Center; WLE: Wide local excision; RV: Radical vulvectomy; RT: Radiotherapy; NED: No evidence of disease; LR: Local recurrence; DM: Distant metastases; Parentheses = %.

Table 4. — Bartholin gland carcinoma (MDACC 1978-1990): Analysis of patients (Treatment, Outcome, Survival Duration)

Patient	Stage	Treatment	Outcome	Survival Duration (months)
VMC	IVA	WLE	Died of DM	7
JC	III	WLE	NED	154+
AM	III	WLE	NED	144+
WS	III	WLE	NED	96+
LZ	III	WLE	NED	120+
EP	III	WLE	NED	180+
MC	III	WLE	NED	156+
GS	III	WLE	NED	132+
AJC	III	RV	Died with NED	72
ES	III	RV	NED	168+
RH	III	RV	NED	150+
DW	III	RV	NED	168+
SM	III	RV	NED	108+
LC	III	RV	Died of DM	24
SP	III	RV	NED	78+
JM	III	RV	NED	168+
IC	III	RT	Died with NED	72
AJ	IVA	RT	Died of DM	20

MDACC: M. D. Anderson Cancer Center; WLE: Wide local excision; RV: Radical vulvectomy; RT: Irradiation alone; DM: Distant metastasis; NED: No evidence of disease.

Local control: The rate of local tumor control was 100% for all three treatment groups (Table 5). There were no significant differences among the treatment groups in rate of primary tumor control or 5-year disease-free survival rate (p=0.1300).

Table 5. — Bartholin gland carcinoma (MDACC 1978-1990): Long-term results by treatment group

Variables for 5 years	Group I WLE + RT (n:7)	Group II RV + RT (n:9)	Group III RT alone (n:2)	Total Group (n:18)
Local control	100%	100%	100%	100%
Disease-free survival	86%	78%	50%	83%

MDACC: M. D. Anderson Cancer Center; WLE: Wide local excision; RV: Radical vulvectomy; RT: Radiotherapy.

Outcome by treatment group: Table 6 shows the causes of death by treatment group: 13 of 18 patients are alive. Of the five who died, three died of distant metastases, and two had no evidence of disease and died of other causes.

Analysis of Complications: Moderate and severe complications were analyzed by treatment group (Table 7). All the treatments were well tolerated by most patients. In patients receiving RT after RV, lymphadema was the complication recorded most frequently (44%). Only one serious vascular complication (abdominal wall necrosis) developed in a patient treated with RV followed by RT.

Table 6. — Carcinoma of the Vulva (MDACC 1978-1990): Causes of death by treatment group

	WLE+ Postop RT (n:7)	RV+ Postop RT (n:9)	RT alone (n:2)	Total Group (n:18)
LR	—	—	—	—
DM	1	1	1	3 (60)
LR+DM	—	—	—	—
NED-other causes	—	1	1	2 (40)

MDACC: M. D. Anderson Cancer Center; WLE: Wide local excision; RV: Radical vulvectomy; RT: Radiotherapy; LR: Local recurrence; DM: Distant metastasis; NED: No evidence of disease; Parentheses = %.

Table 7. — Bartholin gland carcinoma (MDACC 1978-1990): Moderate and severe complications by treatment group

	Group I WLE + RT (n:7)	Group II RV + RT (n:9)	Group III RT alone (n:2)	Total Group (n:18)
Skin necrosis	—	1	—	1 (5.5)
Wound breakdown	—	1	—	1 (5.5)
Wound infection	—	2	—	16 (11.1)
Lymph-edema	2	4	—	6 (33.3)
Lymph-cyst	1	—	—	1 (5.5)
Lymph-angitis	—	1	—	5 (5.3)
Chronic ulcer	2	2	1	5 (27.7)
Vulvar stricture	3	2	1	1 (33.3)
Vascular Complication (Abdominal wall necrosis)	—	1	—	1 (5.5)

MDACC: M. D. Anderson Cancer Center; WLE: Wide local excision; RV: Radical vulvectomy; RT: Radiotherapy; Parentheses = %.

Discussion

Primary carcinoma of the Bartholin gland has been reported in patients as young as 18 years and as old as 91 years (mean, about 52 years) [12]. Adenocarcinoma and squamous cell carcinoma are the most common types of

Bartholin gland carcinomas, representing 87% of cases [3]. Of our study patients, 67% had squamous cell carcinoma and 33% had adenocarcinoma.

The original diagnostic criteria for Bartholin gland carcinoma were described by Honan in 1987 [13]. These criteria included: (1) correct anatomic position of the tumor, (2) intact overlying skin, (3) location of the tumor deep in the labia majora, and (4) the presence of some normal glandular elements. However, advanced Bartholin gland tumors with ulceration of the skin or tumors that completely replace the normal elements of the gland fail to meet these criteria. Thus, new criteria were developed by the Armed Forces Institute of Pathology and recently were advocated by Copeland *et al.* [4]. These new criteria include: (1) areas of apparent transition from normal to neoplastic elements, (2) histologic tumor type consistent with a Bartholin gland origin, and (3) no evidence of a concurrent primary tumor elsewhere.

Although the traditional therapy for Bartholin gland carcinoma and vulvar cancer was RV plus bilateral lymph node dissection, less radical surgery combined with RT has been used as an alternative approach more recently [3, 4, 6, 7]. The role of RT as primary therapy for vulvar cancer has been considered to be limited, but the incidence of locoregional recurrence can be reduced using RT for locally extensive disease [3, 4, 6, 7, 14, 15]. After the primary tumor has been removed completely, the subclinical disease is treated with 45-50 Gy doses of RT [16]. Microscopically positive surgical margins or a large tumor necessitates higher doses (65-70 Gy) [6, 7]. Usually, RT, including 45-50 Gy to the vulva and inguinal lymph nodes plus a boost dose to the abdomen with electron beam therapy (6-9 MV) or an interstitial implant, is effective in controlling disease in the vulva and inguinal-femoral areas [6, 7, 17].

The largest series of Bartholin gland carcinoma cases included 36 patients treated with hemivulvectomy or radical vulvectomy followed by RT, reported by Copeland *et al.* [4]. In that study, 24 patients underwent radical vulvectomy and 12 patients underwent hemivulvectomy followed by lymph node dissection. That was the first study to report the use of less radical surgery such as hemivulvectomy combined with RT for this disease. However, in that study, the RT procedures and the complications of two different surgical techniques used were not described clearly. Of those 36 patients, nine had stage I disease, 15 had stage II disease, ten had stage III disease, and two had stage IV disease. Thirty of the 36 patients underwent lymph node dissection and 14 had nodal metastases. One of the 14 patients who received RT and six of 22 patients who did not developed local recurrences. The 5-year reported survival rate was 84%.

To our knowledge, our report is the second largest study on this topic after Copeland's study. However, we used much less extensive surgery, such as WLE followed by RT, and obtained excellent long-term survival and less morbidity than with more radical procedures. In our report of 18 patients, nine received RV, seven had WLE, and two had RT alone. All the patients received RT after surgery. Fourteen patients had stage III disease, two stage

II disease, and two stage IV disease. Eleven of 18 patients underwent lymphadenectomy, and six had nodal metastases. The 5-year disease-free survival rate was 86% in patients undergoing WLE compared with 78% in patients undergoing RV. The rate of morbidity was lower in patients treated with WLE. There were no local recurrences in any treatment group.

Radiotherapy with external and interstitial irradiation plays a very important role in the treatment of advanced primary carcinoma of the Bartholin gland. This therapy allows the use of less radical surgery with consequent reduced morbidity and good survival. The present study demonstrated that WLE followed by RT is the best treatment approach for advanced primary carcinoma of the Bartholin gland, producing excellent long-term survival and fewer complications.

Acknowledgment

The authors thank Diane S. Rivera for editing the manuscript.

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